

WE CLAIM:

1. A method of treating lupus erythematosus in a mammal with that disease comprising administering to the mammal a physiologically effective amount of an inhibitor of PDE2 wherein said inhibitor does not substantially inhibit COX I or COX II.

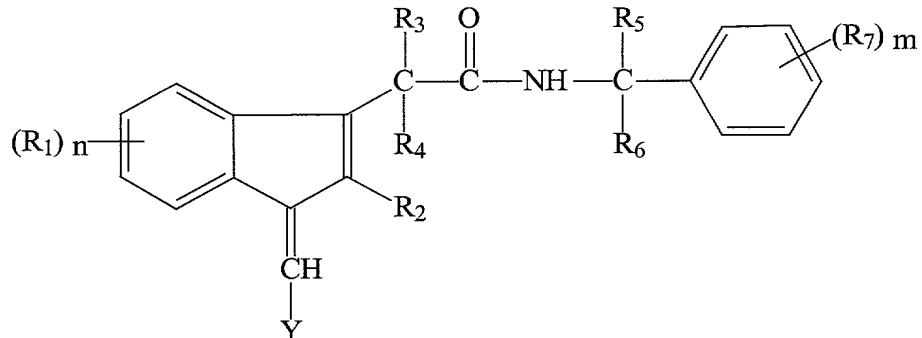
2. The method of claim 1 wherein mammal is also administered an inhibitor of PDE5.

3. The method of claim 2 wherein said inhibitor of PDE2 and PDE5 comprise the same compound.

4. The method of claim 1 wherein said inhibitor is administered without an NSAID.

5. The method of claim 2 wherein said inhibitor IC₅₀ for PDE2 of no more than about 25 μ M. and has an IC₅₀ for each of the COX enzymes greater than about 40 μ M.

6. A method of treating lupus erythematosus in a mammal comprising administering to the mammal a compound of the formula:



wherein R₁ is independently selected in each instance from the group consisting of hydrogen, halogen, lower alkyl, loweralkoxy, amino, loweralkylamino, di-loweralkylamino, loweralkylmercapto, loweralkyl sulfonyl, cyano, carboxamide, carboxylic acid, mercapto, sulfonic acid, xanthate and hydroxy;

R₂ is selected from the group consisting of hydrogen and lower alkyl;

R₃ is selected from the group consisting of hydrogen, halogen, amino, hydroxy, lower alkyl amino, and di-loweralkylamino;

R₄ is hydrogen, or R₃ and R₄ together are oxygen;

R₅ and R₆ are independently selected from the group consisting of hydrogen, lower alkyl, hydroxy-substituted lower alkyl, amino lower alkyl, lower alkylamino-lower alkyl, lower alkyl amino di-lower alkyl, lower alkyl nitrile, -CO₂H, -C(O)NH₂, and a C₂ to C₆ amino acid;

R₇ is independently selected in each instance from the group consisting of hydrogen, amino lower alkyl, lower alkoxy, lower alkyl, hydroxy, amino, lower alkyl amino, di-lower alkyl amino, amino lower alkyl, halogen, -CO₂H, -SO₃H, -SO₂NH₂, and -SO₂(lower alkyl);

m and n are integers from 0 to 3 independently selected from one another;

Y is selected from the group consisting of quinolinyl, isoquinolinyl, pyridinyl, pyrimidinyl, pyrazinyl, imidazolyl, indolyl, benzimidazolyl, triazinyl, tetrazolyl, thiophenyl, furanyl, thiazolyl, pyrazolyl, or pyrrolyl, or substituted variants thereof wherein the substituents are one or two selected from the group consisting of halogen, lower alkyl, lower alkoxy, amino, lower alkylamino, di-lower alkylamino, hydroxy, -SO₂(lower alkyl) and -SO₂NH₂; and

pharmaceutically acceptable salts thereof.

7. The method of claim 6 wherein Y is selected from pyridinyl or quinolonyl.

8. The method of claim 6 wherein R₁ is selected from the group consisting of halogen, lower alkoxy, amino, hydroxy, lower alkylamino and di-loweralkylamino.

9. The method of claim 8 wherein R₁ is selected from the group consisting of halogen, lower alkoxy, amino and hydroxy.

10. The method of claim 6 wherein R₂ is lower alkyl.

11. The method of claim 9 wherein R₂ is lower alkyl.

12. The method of claim 6 wherein R₃ is selected from the group consisting of hydrogen, halogen, hydroxy, amino, lower alkylamino and di-loweralkylamino.

13. The method of claim 9 wherein R₃ is selected from the group consisting of hydrogen, halogen, hydroxy, amino, lower alkylamino and di-loweralkylamino.

14. The method of claim 13 wherein R₃ is selected from the group consisting of hydrogen, hydroxy and lower alkylamino.

15. The method of claim 13 wherein R₃ is selected from the group consisting of hydrogen, hydroxy and lower alkylamino.

16. The method of claim 6 wherein R₅ and R₆ are independently selected from the group consisting of hydrogen, hydroxy-substituted lower alkyl, amino lower alkyl, lower alkylamino-lower alkyl, lower alkyl amino di-lower alkyl, -CO₂H, -C(O)NH₂.

17. The method of claim 15 wherein R₅ and R₆ are independently selected from the group consisting of hydrogen, hydroxy-substituted lower alkyl, amino lower alkyl, lower alkylamino-lower alkyl, lower alkyl amino di-lower alkyl, -CO₂H, -C(O)NH₂.

18. The method of claim 6 wherein R₅ and R₆ are independently selected from the group consisting of hydrogen, hydroxy-substituted lower alkyl, lower alkyl amino di-lower alkyl, -CO₂H, -C(O)NH₂.

19. The method of claim 17 wherein R₅ and R₆ are independently selected from the group consisting of hydrogen, hydroxy-substituted lower alkyl, lower alkyl amino di-lower alkyl, -CO₂H, -C(O)NH₂.

20. The method of claim 6 wherein R₇ is independently selected in each instance from the group consisting of hydrogen, lower alkoxy, hydroxy, amino, lower alkyl amino, di-lower alkyl amino, halogen, -CO₂H, -SO₃H, -SO₂NH₂, amino lower alkyl, and -SO₂(lower alkyl).

21. The method of claim 19 wherein R₇ is independently selected in each instance from the group consisting of hydrogen, lower alkoxy, hydroxy, amino, lower alkyl amino, di-lower alkyl amino, halogen, -CO₂H, -SO₃H, -SO₂NH₂, amino lower alkyl, and -SO₂(lower alkyl).

22. The method of claim 6 wherein R₇ is independently selected in each instance from the group consisting of hydrogen, lower alkoxy, hydroxy, amino, halogen, -CO₂H, -SO₃H, -SO₂NH₂, amino lower alkyl, and -SO₂(lower alkyl).

23. The method of claim 18 wherein R₇ is independently selected in each instance from the group consisting of hydrogen, lower alkoxy, hydroxy, amino, halogen, -CO₂H, -SO₃H, -SO₂NH₂, amino lower alkyl, and -SO₂(lower alkyl).

24. The method of claim 22 wherein at least one of the R₇ substituents is ortho- or para-located.

25. The method of claim 23 wherein at least one of the R₇ substituents is ortho- or para-located.

26. The method of claim 24 wherein at least one of the R₇ substituents is ortho-located.

27. The method of claim 25 wherein at least one of the R₇ substituents is ortho-located.

28. The method of claim 6 wherein Y is selected from the group consisting of quinolinyl, isoquinolinyl, pyridinyl, pyrimidinyl and pyrazinyl or said substituted variants thereof.

29. The method of claim 6 wherein said compound comprises (Z)-5-fluoro-2-methyl-(4-pyridylidene)-3-(N-benzyl)indenylacetamide hydrochloride.

30. The method of claim 6 wherein said compound comprises (Z)-5-fluoro-2-methyl-(4-pyridylidene)-3-(N-benzyl)-indenylacetamide p-methylbenzenesulfonate.

31. A method of inhibiting activated macrophages in a mammal with lupus erythematosus comprising chronically administering to the mammal a physiologically effective amount of an inhibitor of PDE2.

32. The method of claim 31 wherein mammal is also administered an inhibitor of PDE5.

33. The method of claim 32 wherein said inhibitor of PDE2 and PDE5 comprise the same compound.

34. The method of claim 31 wherein said inhibitor does not substantially inhibit COX I or COX II.

35. The method of claim 33 wherein said inhibitor does not substantially inhibit COX I or COX II.

36. The method of claim 31 wherein the mammal is a companion pet.

37. The method of claim 36 wherein the mammal is human.

38. A method of treating lupus erythematosus in a mammal with that disease comprising inhibiting PDE2 in the diseased tissue without substantially inhibiting COX I or COX II.

39. A method of inhibiting activated macrophages in a mammal with rheumatoid arthritis comprising chronically administering to the mammal a physiologically effective amount of an inhibitor of PDE2 having a PDE2 IC₅₀ no more than about 25 μ M and having a COX IC₅₀ greater than about 40 μ M.